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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Robert E. Reiter, et al.
Serial No.:	Examiner: Larry R. Helms, Ph.D.
Filed:	Group Art Unit: 1642
Title:	

55 S. Lake Avenue, Suite 710
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Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

DECLARATION OF STEVEN B. KANNER, PH. D.

I, Steven B. Kanner, declare as follows:

I am Director of Cancer Research at Agensys, Inc. In this position I direct research and development to identify and validate novel cancer targets. In addition, I oversee research and development of new cancer therapeutics and diagnostics involving these targets. Accordingly, we investigate the effects of specific genes and gene products on tumor development, growth, and progression. I regularly attend national and international conferences addressing issues in cancer research, conferences where established as well as cutting edge ideas are presented.

I have a Ph.D. in Immunology and Microbiology from the University of Miami, Miami, Florida. In addition, I completed a postdoctoral fellowship at the University of Virginia. I have worked in the field of molecular biology at a doctoral level for over 17 years. Accordingly, I have extensive experience in novel target identification and validation, assay development and small molecule drug discovery, with particular

expertise in oncology, immunology and inflammation. A copy of my *curriculum vitae* is attached as Exhibit A.

I understand that the U.S. Patent 5,836,136 to Au Young (the "Au Young patent") has been cited as disclosing to the scientific community various aspects related to the Prostate Stem Cell Antigen (PSCA). I have reviewed the Au Young patent in detail. Sequences in Au Young that align with PSCA are called SCAH-2 in that document.

Furthermore, I understand that the earliest filing in the PSCA patent family is 10 March 1997. I also understand that patentability is determined as of an application's filing date. Accordingly, in this Declaration I will discuss the Au Young patent for the level of prior art it would have provided to typically skilled persons in my technical area as of 10 March 1997.

I understand that an "invention" must be sufficiently concrete so that it can be described so that the world can appreciate the specific nature of the work that sets it apart from what was before. An inventor must be able to describe the subject to be patented with such clarity that the reader is assured that the inventor actually has possession and knowledge of the unique composition or method. Further, I understand that a prior art disclosure must set forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed. Such information Au Young fails to provide.

The citation of Au Young as prior art *requires that* there be a gene and protein in nature. Without existence of a protein, it is impossible make any conclusion regarding whether subject matter is disclosed to the art. Accordingly, the Au Young disclosure does not provide the elements of the antibody compositions presently claimed, and does not allow one of skill in the art to practice the present invention.

What the reader learns from the Au Young patent is a wish or plan or first steps for obtaining a desired result. As one of ordinary skill in the art in March 1997, it is apparent that Au Young had a goal for achieving certain end results. However, Au Young had not proceeded to do what was necessary to accomplish the desired end.

Au Young had made some relevant explorations in this field. However, the meaning these explorations would have had in March 1997 was not significant. I understand that Au Young is not to be viewed in hindsight, in view for example of Applicants discovery of PSCA. Instead, Au Young should be considered as it would have been in the context of March 1997.

As of March 1997, Au Young contemplated that there *may* be a SCAH-2 gene in nature, there *may* be a SCAH-2 protein, and contemplated that the protein *may* have some sort of function or disease correlation. These are steps in the discovery process. What Au Young *did not do*, however, is succeed in taking the basic and critical steps of actually isolating such a gene, finding such a protein, identifying any meaning to such protein, or raising antibodies to any such protein. Absent these steps, Au Young's explorations, interesting though they might be through hindsight, did not constitute a complete, described and usable discovery.

The Au Young disclosure concerning SCAH-2 was hypothetical. Au Young lacks any actual data on SCAH-2. There was no demonstration of actual possession of SCAH-2. Further, Au Young did not provide any understanding that a SCAH-2 gene and protein are truly in nature or that it is expressed in any manner. One of ordinary skill in March 1997 would not know or expect that any such information does exist except through subsequent trial and error, which hardly suggests possession of any complete discovery or invention by Au Young.

I understand that the patent statutes require a patentee to "show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention , and that a disclosure must show that an inventor had invented each feature that is included as a claim limitation. Even if Au Young was reasonably certain that the necessary materials existed and could eventually be found, there was no showing in the patent that she knew such to be facts, neither were these facts known in the art.

I understand that an applicant must convey with reasonable clarity to those skilled

in the art that, as of the filing date sought, he or she was in possession of the invention".[1] I further understand that a disclosure is not sufficient if one of ordinary skill in the art must first make the patented invention before he can ascertain the claimed features of that invention.[2] The Au Young disclosure did not convey with reasonable clarity to those skilled in the art, as of March 1997, that she was in possession of SCAH-2 gene, protein, relevant protein expression or function or any antibodies specific to SCAH-2. One of skill in the art in March 1997 would have needed to first make the SCAH-2 subject matter of Au Young before they could ascertain the claimed features of that "invention" or attribute any meaning to that disclosure.

At most, the Au Young disclosure amounts to the need for trial and error. Au Young was at best a starting point, a potential direction for further discovery research. Appreciating a starting point is essentially the initial step in a research plan. However, cutting against an interpretation of Au Young as a research plan, is that Au Young did not even describe the importance of confirming the existence of the gene and protein in nature. The patent does not even deal with the important scientific issues of whether the SCAH-2 gene and protein may be bioinformatic artifacts. If one does not appreciate that their data is uncertain, it calls into question any conclusions they make about it.

The SCAH-2 subject matter of Au Young cannot be practiced until one discovers actual existence and relevant expression of that subject matter. However, in March 1997 such information was neither disclosed by Au Young nor otherwise known in the art.

Thus, to practice the subject matter in the Au Young disclosure, a person of ordinary skill in the art would have to engage in experimentation, with neither assurance nor a reasonable expectation of success. Reasonable detail is lacking in Au Young that would have enabled members of the public to attribute any meaning and thus carry out the "invention."[3] One of skill could not have carried out an invention that was not known to exist.

As noted, no gene or protein or expression in nature was known in the art or

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[1] *See* Vas-Cath, 935 F.2d 1555, 1563-64

[2] *New Railhead Mfg.*, 298 F.3d at 1295

[3] Id.

disclosed by Au Young, the SCAH-2 data was bioinformatic and prophetic. Au Young then describes some of the steps to be taken *when* such crucial elements and expression data are identified. What was missing was the necessary link between those two steps: actually finding the SCAH-2 gene and protein in nature, and identifying relevant protein function or expression. Au Young only discloses general ideas that may or may not be workable. What Au Young omits is not minor detail. Missing data include crucial information of existence and ability to use a gene, protein and antibodies to the protein.

Turning now to the Office's rejections under Au Young. These rejections are credible only when predicated on several serial assumptions. The assumptions that must underlay the rejections are that concerning SCAH-2, persons of ordinary skill in the art would have believed that:

1) Au Young disclosed a nucleic acid assembly that actually occurs in nature.

2) Au Young meaningfully appreciated the correct reading frame for Applicants' PSCA protein.

3) Au Young actually intended a particular protein as SCAH-2. Au Young ambiguously referred to several amino acid sequences.

4) A protein was truly encoded by said reading frame, i.e., that it was not a pseudogene.

5) Any such protein was so meaningful that antibodies would be raised to it.

6) Every possible antibody was, in fact, raised, or that one might have raised an antibody that might have had the properties of the present claims.

Far too much is missing from Au Young to have made the above assumptions credible to one of ordinary skill in the art in March 1997.

Au Young lists a hypothetical gene, SCAH-2, which was a nucleotide assembly. This assembly was constructed from two different tissues, tissues that were at two

different states of neoplasia.[4] Au Young never constructed a gene or protein, and never confirmed the existence of any gene or protein in nature. By necessity, she never made any SCAH-2 deposit in a public depository. The Au Young disclosure lacks any tissue distribution, or cancer-association data. Neither the gene nor protein in Au Young was a fully defined sequence. Thus, neither the SCAH-2 gene nor protein set forth in Au Young match the respective true PSCA sequence consequent to sequence errors, gaps and unknown sequence positions. There was very unclear disclosure of any SCAH-2 open reading frame (ORF). No data ruled out that any SCAH-2 "gene" is actually a pseudogene. "It is important to characterize the human processed and nonprocessed pseudogene populations as their existence interferes with gene identification and prediction (particularly nonprocessed pseudogenes or individual pseudogenic exons.)"[5] This principle was known in March 1997, however nothing in the Au Young disclosure or otherwise available in the art in March 1997 manifested to one of skill in the art that Au Young had a SCAH-2 gene, protein or antibody having the limitations set forth in her application. Nothing was isolated and/or purified, and nothing was deposited with a public depository. There is no actual data that correlates any SCAH-2 protein with any disease, and no actual data on any protein function. Au Young made no antibodies whatsoever. No elements of the present claims were placed in the art by the publication of Au Young. Collectively, there was no motivation to make antibodies that immunospecifically recognized and bound PSCA or fragments thereof.

The six assumptions that underlie rejection of the present claims based on Au Young will now be addressed.

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[4] One component is bladder tumor (Au Young '391, col. 4, lines 27-29, col. 5, lines 1-18) and the other is some sort of uterus tissue, presumed to be normal for lack of any other description (Au Young '391, col. 4, lines 27-29).

[5] See, e.g., Harrison et al., Genome Res 12:272-280 (2002). The statement by Harrison et al. reflects an issue also known in March 1997.

1. **Assumption: That Au Young disclosed a nucleic acid assembly that actually occurs in nature.**

   Fact: No nucleic acid sequence in nature was ever documented by Au Young; the sequence itself is incomplete and not fully sequenced.

As viewed in March 1997, Au Young lacked data on any SCAH-2 (or PSCA) gene. The Au Young disclosure merely lists a hypothetical gene which was a nucleotide assembly sequence.[6] The SCAH-2 nucleic acid assembly was derived from six overlapping nucleic acid fragments isolated from two distinct tissues, and of two states of neoplasia.[7] As a consequence of the fact that Au Young never documented a gene (or protein), the disclosure lacks any tissue distribution, or disease-association data.

A conclusion that there is a SCAH-2 gene in nature was neither disclosed nor credibly supported in March 1997. Asserting existence of a gene in nature on the basis of a fragment assembly is highly suspect for a number of reasons.[8] For example:

- One or more of the short fragments used to construct the SCAH-2 assembly could have sequence errors, making the assembly and subsequences thereof artifacts.
- The fragments could contain or be contaminant sequence such as vector, linker, or virus.

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[6] One component is bladder tumor (Au Young '391, col. 4, lines 27-29, col. 5, lines 1-18) and the other is some sort of uterus tissue, presumed to be normal for lack of any other description (Au Young '391, col. 4, lines 27-29).

[7] Au Young '136, column 4, lines 50-59. These clones are designated in Au Young as SEQ ID NOS: 21-26. Thus, the Au Young nucleic acid assembly sequence was made using:

SEQ ID 21—normal uterus library
SEQ ID 22—normal uterus library
SEQ ID 23—bladder tumor library
SEQ ID 24—bladder tumor library
SEQ ID 25—bladder tumor library; and
SEQ ID 26 —bladder tumor library

[8] See, e.g., Sorek and Safer, "A Novel Algorithm for Computational Identification of Contaminated EST Libraries" Nucl. Acids Res. 31(3): 1067-1074 (2003)

- The fragments could be chimeric sequences. A chimera is a concatenation of two or more expressed sequences from different areas. If a chimera is used it will likely result in combination of two genes into a single incorrect gene prediction.
- ESTs can also be a contaminant of genomic DNA from the organism itself. Genomic contaminants can make introns appear to be expressed.
- Even if an individual nucleic acid fragment used in the assembly does code for a protein, that protein may not be SCAH-2. Instead, the EST could be spliced into a variant gene that codes for some other protein.
- Since the fragments used to construct the assembly came from two tissues, it is possible that the "gene" does not actually exist in either one of those tissues.
- Premature mRNA (pre-mRNA), i.e., mRNA that did not undergo splicing is another form of EST contamination; in this situation intronic sequences will falsely appear to be exons. (Additionally, as discussed below, even if the assembly occurs in nature, it may not be a gene at all but a pseudogene).

The SCAH-2 assembly was never cloned at all, let alone cloned in a confirmatory manner that shows a full length gene.[9] Furthermore, the SCAH-2 nucleotide sequence (SEQ ID NO: 4 of Au Young) is incomplete and not fully sequenced. The nucleic acid sequence of SCAH-2 was incomplete in several respects. It had an unknown (labeled "N") at nucleic acid position 475, and listed five (5) positions on a 50% chance basis.

I note that SCAH-2 differs from human PSCA at both the nucleic acid sequence and amino acid sequence levels. The PSCA genomic sequence is 990 nucleotides, whereas SCAH-2 is 494. The nucleic acid sequence of Au Young matches PSCA at only 482 of its 494 bases (97%), and aligns with less than 50% of the PSCA sequence. Additionally, three gaps along the 494 nucleotide match range are created to achieve the

[9] For example, from multiple identified hits obtained by probing a sequence library with probes derived from the putative nucleic acid assembly sequence, or by PCR.

alignment. Even with the gaps, compared to PSCA the SCAH-2 nucleic acid sequence is inaccurate at nine (9) positions.[10]

In view of the varied tissue sources and neoplastic statuses of the constituent elements of the Au Young nucleic acid assembly, the lack of any confirmatory cloning data, and lack of any information that constituent fragments were not contaminant or artifact, the scientific meaning, if any, that one of ordinary skill would attribute to the SCAH-2 assembly is exceedingly low. It is scientifically possible and not in any way ruled out, that the sequence was merely a bioinformatic artifact, and not in nature at all. Thus, in March 1997 it was not scientifically prudent to conclude that the SCAH-2 assembly actually occurred in nature; one of ordinary skill in the art would not have made such a conclusion.

In March 1997 one of ordinary skill would not have concluded that Au Young disclosed a nucleic acid sequence that actually occurs in nature. Thus, as of March 1997 one of skill would *not* have interpreted Au Young to have actually disclosed the PSCA nucleic acid sequence.

2. **Assumption: That a protein was truly encoded by a/the SCAH-2 nucleic acid sequence, i.e., that it was a gene and not a pseudogene.**

   Fact: No SCAH-2 protein was ever documented by Au Young.

There is no data whatsoever in Au Young that a SCAH-2 protein was actually produced in nature. It is entirely possible that even if there were a SCAH-2 nucleic acid sequence in the human genome, that there was no actual coding gene at all and thus no corresponding protein. This important possibility severely undercuts any scientific meaning that would have been attributed to Au Young concerning any SCAH-2 protein in March 1997.

Not only could a putative gene having a methionine codon followed by a downstream stop codon be a "false" gene because it encodes no RNA at all, a gene that encodes RNA can be a pseudogene because the RNA is degraded before it is translated

[10] The SCAH-2 protein predicted by Au Young is labeled "Xaa" at our amino acid position 94 for unknown or unidentified.

into protein, the gene can be derived from reverse transcription of mRNA followed by reintegration into the genome "retropseudogenes" with accompanying degradation and disablements[11], the gene can be derived from a duplication of an original gene followed by an initial coding disablement, potentially followed by further coding disablements.[12]

The Au Young disclosure provides a hodgepodge of inconclusive and oftentimes ambiguous information. Thus, one of ordinary skill would have looked on the Au Young disclosure regarding any SCAH-2 protein with substantial uncertainty. As of March 1997 one of skill would *not* have interpreted Au Young to have actually disclosed the PSCA protein sequence. The only certainty as to any SCAH-2 protein in nature is provided in hindsight by use of the information provided in Applicants' disclosure.

At most, Au Young *might* have constituted an invitation for further experimentation in an attempt to arrive at information possessed of scientific credibility. However, as discussed below, the ambiguities in Au Young undercut even that motivation.

3. **Assumption: That Au Young meaningfully appreciated the actual sequence of Applicants' PSCA protein.**

   Fact: Au Young ambiguously referred to several amino acid sequences, some based on an open reading frame and others not; it is not clear what SCAH-2 protein sequence is actually intended by the Au Young disclosure.

Upon careful review of the Au Young disclosure as a whole, the existence and composition of any SCAH-2 amino acid sequence is even more unclear than is the nucleic acid sequence. Several amino acid sequences set forth in Au Young any one, or even all, of which could have been what she intended as "a" or "the" SCAH-2 protein:

- Figure 2 of Au Young provides an amino acid sequence that was deduced from her entire nucleotide assembly. This sequence has 164 amino acids. No reading frame was appreciated. The alignment of PSCA is embedded within the Figure 2 SCAH-2

[11] see, e.g., Harrison et al., Genome Res 12: 272-280 (2002)
[12] see, e.g., Harrison et al., Genome Res 12: 272-280 (2002)

sequence. This SCAH-2 protein does not begin with a start methionine, as would prudently be done when no upstream stop codon was identified; the sequence continues past a stop codon as would prudently be done when there is uncertainty as to the accuracy of the sequence data.

- The protein in Au Young Figure 2 was designated SEQ ID 2 but was inaccurately set forth in her Sequence Listing, it does not match the Figure.[13] This sequence begins with a methionine and has 123 amino acids. The Au Young sequence listing was not proper since it was supposed to have forth the same sequence as the figure. Since the SEQ ID 2 entry is not correct, it undercuts the scientific value one would attribute to it. If anything, one of ordinary skill would disregard the amino acid sequence in the improper computer-based listing.
- Column 4, lines 62-65 states, "SCAH-2 has 27% identity to chicken stem cell antigen 2, is 123 amino acids long, and contains three potential glycosylation sites at N40, N83, and N96." This protein length conflicts with Figure 2, but the length does correspond to her SEQ ID 2. However, the three specified asparagines do not match either of these sequences, nor do they match any sequence Applicants could find in the Au Young document.
  - If she meant SCAH-2 of Figure 2, none of the asparagines matched, and the "X" at position 96 is supposed to be asparagine and not unknown.
  - If she meant the SCAH-2 protein in the Sequence Listing as SEQ ID 2, the asparagines at 40 and 83 match, position 94

[13] The *nucleic* acid sequence from Figure 2 does appear to match Au Young sequence listing SEQ ID NO 4.

is unknown, and position 96 is not glycine but an asparagine.

- If her sentence from Column 4 is meant to refer to the chicken stem cell antigen-2 (Sca-2, her SEQ ID 20) the length is off by 3 amino acids 123 vs. 126, the two asparagines at 40 and 83 do not match, but the asparagine at position 96 does match.

Taken as a whole concerning SCAH-2, Au Young ambiguously referred to at least six sequences, four permutations of which might be SCAH-2. As viewed in March 1997, one of skill in the art would have no way of knowing which are erroneous. In fact, it is only hindsight in view of Applicants' disclosure that allows one to attribute the status of "erroneous" to the SCAH-2 sequences. In March 1997, the most Au Young would be viewed as disclosing is a research goal, an invitation for experimentation to confirm a gene and protein. As disclosed in Au Young and without use of hindsight direction based on Applicants' PSCA, Au Young did not provide any particular protein sequence meaningfully described as SCAH-2, and certainly not the exact sequence of PSCA.

Only hindsight motivates one to, amongst the various SCAH-2 related protein disclosure,

1) select only the 123 amino acid permutations;

2) decide what Au Young did not do about amino acid position 94, which she considered unknown,[14] turn to the nucleic acid sequence, use the two possible codons based on the "S" in the nucleic acid sequence, identify that these code for either alanine (GCC) or glycine (GGC);

3) select alanine and not glycine at position 94; and,

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[14] Applicants know of no principle that places authority on later individuals to answer why an earlier publication lacked information and/or resolve inconsistencies. Rather, Applicants submit that it is improper hindsight to fill in blanks after the fact. It is no more appropriate to attribute dominant meaning to the nucleic acid sequence and fill in the gap in the amino acid sequence with two alternatives (glycine or alanine), than it is to attribute dominant meaning to the unknown in the amino acid sequence and say that the corresponding codon was not known. Perhaps the "S" in the nucleic acid sequence was a typographical error; this is consistent with her amino acid sequences.

4) disregard Au Young at Column 4, lines 62-65 that SCAH-2 has asparagine at position 96 and use glycine instead.

Of the alternative SCAH-2 proteins some are at least 164 amino acids long, and others are 123 amino acids long. Amongst these alternatives Au Young did not know the identity of the amino acid at position 96 in her at least 164 amino acid proteins, and position 94 in her 123 amino acid proteins, nor the actual codon[15] that corresponded to that position. Only hindsight provides the a possible identity of amino acid at this position by reviewing the corresponding codons, and this hindsight gives ascendant meaning to the nucleic acid sequence over the amino acid sequence. However, Au Young did not do this herself in any of the assorted amino acid discussions or sequences in her document. To one of ordinary skill in March 1997, Au Young did not clearly disclose a SCAH-2 protein and did not disclose the PSCA protein. Furthermore, in March 1997, one would not have been motivated to choose amongst the disclosure of Au Young and arrive at the PSCA protein. Due to the lack of fundamental gene discovery, there was no reasonable expectation that any SCAH-2 protein existed at all, let alone a permutation that matches PSCA.

It is not evident that Au Young was clear on an ORF for her SCAH-2 protein. Only hindsight, based on reviewing applicants' disclosure, resolves these ambiguities. However, I understand that hindsight is not permitted in a proper patentability assessment of applicants' claims.

4. **Assumption: That Au Young actually had a particular open reading frame for a SCAH-2 protein.**

Fact: It is ambiguous whether Au Young was certain of any open reading frame in her nucleic acid sequence. No amino acid sequence in nature was ever documented by Au Young.

Each of the various SCAH-2 proteins in the Au Young patent was a deduced sequence. Reviewing her disclosure, as it would have been interpreted in March 1997 and without hindsight, it appears that either Au Young had not arrived at any SCAH-2

[15] The Au Young codon at positions 286-288 of Figure 2 is GSC. The IUPAC definition for "S" is C or G.

open reading frame at all, or if she did, was not sure she had a sufficiently valid nucleic acid sequence to make it credible. Once again, I understand that hindsight is not to provide the certainty that the Au Young disclosure lacked.

The SCAH-2 nucleic acid sequence and its corresponding protein are disclosed by Au Young as being set forth in Figure 2 (col. 5, lines 7-10). The sequence listing for this Figure properly corresponds for the nucleic acids (her SEQ ID 4), but improperly does not correspond for the amino acids (her SEQ ID 2). Inordinate meaning should not be inferred to a clearly improper sequence listing entry. Further, if Au Young at column 4, lines 62-65[16] truly indicates that the SCAH-2 protein is 123 amino acids, the specified asparagines do not match any sequence, and may have been meant to refer to the chicken sequence (her SEQ ID 20).

In March 1997, the Au Young disclosure would have been viewed in its entirety. That Au Young fully deduced the nucleic acid sequence of Figure 2 is consistent with the tentative status of her data. Minimizing the relevance of this now appears to be a hindsight act in view of applicants' PSCA. It was, and still is, scientifically prudent to deduce an entire nucleic acid when one is unclear about the extent (e.g., if an upstream stop codon was not known) or the quality/veracity of the sequence is uncertain or low (e.g., a stop codon may only be a sequence error).

Au Young discloses the following:

- a figure that contains a sequence along with a SEQ ID identifier,
- a sequence listing filed simultaneously with the application, and
- the figure sequence and the corresponding SEQ ID differ.

Under these facts, one of skill would attribute less meaning to the listing than the corresponding sequence in the figure.

[16] The sentence states, "SCAH-2 has 27% identity to chicken stem cell antigen 2, is 123 amino acids long, and contains three potential glycosylation sites at N40, N83, and N96."

As of March 1997 the following would be done upon reading Au Young and seeing that a sequence is referred to in a figure and a SEQ ID identifier is also provided. The figure would be reviewed. It would also be noted that patent authorities require a computer readable Sequence Listing. A scientist properly assumes that an applicant and relevant patent authorities would comply with the Sequence Listing requirements and would, in keeping with regulations, exactly set forth a sequence from a figure or specification in the Sequence Listing. If the scientist does ascertain that the sequence in the figure and the Sequence Listing do not match, between the figure sequence and the SEQ ID sequence, more weight is given to the figure. Moreover, the credibility of all of this information as definitive or meaningful disclosure is lowered. The lack of quality control makes one of skill call into question the apparent accuracy of all other information.

5. **Assumption: That any such SCAH-2 protein was so meaningful that antibodies would be raised to it.**

Fact: No SCAH-2 protein was ever documented by Au Young and no antibodies were raised by Au Young.

Nothing in Au Young indicates that she raised any antibodies to SCAH-2 or deposited any hybridomas that encode such antibodies. Furthermore, in a situation where the following is *not* known:

- whether there is a nucleic acid in nature;
- if there is such a nucleic acid sequence what the open reading frame is;
- if there were a nucleic acid, whether that may be a pseudogene,

one of ordinary skill would not even begin to try to raise antibodies to some protein that may or may not be encoded. In this fact situation, raising of antibodies is not a method by which one would confirm existence of a putative protein. This was true in March 1997 and it is still true today. If one were motivated to conduct research on SCAH-2 due

to Au Young, initial studies would attempt to confirm existence of the nucleic acid sequence, such as by gene cloning.[17]

Where the art is ambiguous, speculative, and lacks even a single working example, there would be no evidence there is a gene or protein at all. A nonexistent protein is not useful and it cannot be described. One of skill in March 1997 would not realistically be able to make antibodies to SCAH-2 since there was no knowledge of what antibodies would be made to. In March 1997 there were no facts, in Au Young or otherwise in the art, that disclosed or permitted one to make or use any SCAH-2 gene, protein, protein expression or any antibodies to any such protein. Fundamental gene and protein discovery is lacking in Au Young and elsewhere in the art in March 1997.

Au Young as Disclosing a Disease Correlation Function for SCAH-2

Furthermore, Au Young did not establish to one of ordinary skill that, if a SCAH-2 protein were to exist, it had any disease-associated meaning that would have made raising antibodies relevant. Concerning both SCAH-1 and SCAH-2 Au Young states:[18]

> The present invention discloses novel human stem cell antigens (SCAH), characterized as having homology to Sca-2. Accordingly, the invention features substantially purified SCAH-1 and SCAH-2, encoded by the amino acid sequences of SEQ ID NO:1 and 2, respectively, and having characteristics of the LY-6 family of cysteine rich proteins which are expressed on the surface of lymphoid cells. ...
>
> The invention further provides diagnostic assays and kits for the detection of naturally occurring SCAH-1 or SCAH-2. It provides for the use of substantially purified SCAH-1 or SCAH-2 as a positive control and to produce anti-SCAH-1 or SCAH-2 antibodies which can be used to quantitate the amount of SCAH proteins in human body fluids or biopsied tissues. ...
>
> Substantially purified SCAH-1 or SCAH-2 or their fragments may be useful as pharmaceutical compositions. For example,

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[17] This could occur, e.g., by cloning the full length gene from a cDNA library derived from a single tissue or cell type.

[18] (Au Young, '391, column 2, lines 12-18, 43-49, 52-55)

> they may be used to inhibit or reverse the development of tumors.

I understand that such passages must be interpreted in light of the overall disclosure of Au Young. Only if taken out of context would this be viewed as conclusive. Nothing here changes my conclusion that in March 1997 nothing Au Young or otherwise in the art disclosed or permitted one to use any SCAH-2 gene, protein, protein expression or any antibodies to any such protein.

I understand that in related prosecution[19] the USPTO has asserted that the Au Young sentence, "[t]he nucleic acid sequence encoding a portion of the novel stem cell antigen homolog-2 (designated in lower case, scah-2) was present in tissues removed from bladder tumor and uterus"[20] teaches treating a patient having bladder tumor, using antibodies against SCAH-2. I disagree: this assertion is not scientifically credible, and would not have been made based on Au Young in March 1997.

One could not in March 1997, or even now, draw scientifically meaningful conclusions from Column 4, lines 27-30 of Au Young. Au Young's detection of portions of SCAH-2 cDNA in bladder and uterus tissues does not describe or suggest correlation of SCAH-2 with cancer in those tissues with any scientific credibility.[21] This reasoning means that every nucleic acid assembly that might possibly encode a protein does encode a protein; if multiple variant proteins could be encoded, they all are; and, that protein is expressed in every tissue from which ESTs were derived. This is not scientifically credible. Au Young does not teach that SCAH-2 protein was observed in bladder tumor. Au Young does not teach that SCAH-2 gene or protein even exits in nature.

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[19] U.S.S.N. 09/963,620, Paper 9, page 22. *Note, the USPTO statement referred to lines 29-30 only of a sentence that extends from lines 27-30. If that portion is taken out of context, it appears to say something quite different that the sentence does properly viewed as a whole.*

[20] Au Young '391 patent, column 4, lines 27-30

[21] The basis for this reasoning, if applied to uterine tissue, seems to be that, upon locating a particular partial gene sequence in a tissue, it becomes scientifically credible that there is cancer in that tissue. In contrast to such an assertion, however, it is a well-recognized characteristic of neoplastic cells that they have deviant characteristics compared to respective normal, non-neoplastic cells. This is particularly true of malignant, cancerous neoplasms.

The fact that the source tissues were from two states of neoplasia teaches away from an idea that the sequence correlated with a particular disease state such as cancer. Au Young merely states that "portions" of the nucleic acid of SCAH-2 were present in tissues removed from bladder tumor. The use of cDNA from bladder and uterus tissue libraries to make the SCAH-2 assembly is as close as Au Young came to actual data. Au Young provides no characterization or expression data on SCAH-2.[22]

Moreover, it appears that the only mention of cancer treatment in Au Young occurs in the context of polynucleotides not protein, generically relates to all polynucleotides in the document, and is a laundry list of potential cancers:[23]

> Therapeutics
>
> The polynucleotides disclosed herein may be useful in the treatment of conditions associated with the tissues used to construct the cDNA libraries (shown in the Sequence ID Listing) which contained partial scah sequences. These include, but are not limited to, conditions such as leukemias and cancers of the bladder, breast, lung, ovary, prostate, and uterus.

The quoted paragraph is about *both* SCAH-1 and SCAH-2. This broad listing of potential cancers certainly does not establish to one of ordinary skill or make obvious to them that these cancers are correlated in any way with either SCAH-1, SCAH-2, or both. There is no reasonable expectation of success that SCAH-1 or SCAH-2 would be found in those assorted tissues.

If SCAH-2 existed in nature, and actually encoded a protein, but without any neoplasia-associated characterization and/or tissue localization data, it could be merely a

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[22] This is precisely a context in which said "portion" may not be expressed in the asserted protein at all, but in a variant thereof.

[23] Au Young '391, column 18, lines 15-21

housekeeping-type gene.[24] Many of the about 30,000 genes in a cell are housekeeping genes. SCAH-2 could be a ubiquitous gene not correlated with cancer in any way.

A conclusion that SCAH-2 is a ubiquitous gene is particularly plausible for SCAH-2, because SCAH-2 was derived from both normal and tumor sources and from two different tissues. Without more data, there was no reason to implicate SCAH-2 in cancer based on the disclosure of Au Young.[25]

These principles are exemplified for the tissues from which fragments were derived to construct the SCAH-2 nucleic acid assembly: normal uterus and bladder tumor. It is not scientifically credible to infer cancer tissue expression based on the EST fragments from normal uterus. Conversely, this argument applies to the bladder tumor component of the nucleic acid assembly. Just because an EST was derived from a tumor cell does not mean it is not in a normal cell. There is not enough scientific information in the mere existence of the nucleic acid assembly in Au Young to determine any malignant or normal expression pattern in any tissue.

Moreover, even if any function or disease association had been documented for SCAH-2, the lack of actual expression data is a serious impediment to an assertion that any antibodies are obvious to one of ordinary skill. Even if the protein exists, it could be expressed at such low levels or turned over so rapidly that raising of antibodies to it is not scientifically relevant, i.e., not an obvious thing to do.

Further, as Au Young only hypothesized and never expressed SCAH-2, no tissue localization/distribution data was possible from Au Young. Au Young had no way to know whether SCAH-2 was expressed at all; was ubiquitous; if expressed, was only on select cells, such as malignant cells; or, if expressed, was overexpressed on any particular tissue. Without localization data, there was no way to know whether SCAH-2 was

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[24] For example, it might exist in cancer tissues or it might not exist in cancer tissues; if it exists in cancer tissues, it might be over expressed in cancer tissues compared to normal tissues or it may not be over expressed in cancer tissues compared to normal tissues.

[25] Moreover, any attempt to correlate SCAH-2 with any other tissue, such as a tissue mentioned at Au Young column 18 is totally specious. Those tissues are components of other nucleic acid assembly sequences of ESTs in the document.

expressed in vital organs such as the heart or lung. Cytotoxic targeting of vital organs is to be avoided on scientific and ethical bases. For example, one would not even consider a treatment without knowing if the treatment itself would be contemplated to kill the patient.

Since SCAH-2 transcripts are found in both normal and tumor cells, and without any actual expression data whatsoever (e.g., upregulation in tumor versus normal, vital organ expression, etc.) Au Young teaches away from using SCAH-2 as a target for cancer therapy. Fundamental discovery regarding disease correlation is lacking. Thus, in the absence of any specific correlation of SCAH-2 with malignant tissues and not with vital organ tissues, it would be scientifically contraindicated and ethically improper to target cells in humans that express SCAH-2.

Au Young as Disclosing Stem Cell Antigen or Ly-6 Function for SCAH-2

As to any functional aspect of SCAH-2, Au Young did not establish to one of ordinary skill that a SCAH-2 protein, if it were to exist, had any particular functional meaning that would have made the raising of antibodies relevant. On the other hand, there is no function-related disclosure, such as motif or alignment identity, that is so compelling that it indicates the protein may truly exist.

Au Young speculated as to two meanings to SCAH-2; neither of these would have been reasonably expected to be true, let alone definitive, as of the filing date of the present invention such that antibodies would be raised.

First, Au Young speculated/concludes that the SCAH-2 protein is a stem cell antigen. That is the basis for her name *S*tem *C*ell *A*ntigen *H*omolog (SCAH).[26] This speculation/conclusion is based on a low identity alignment to a non-mammalian, chicken sequence.[27] The identity was only 27%; moreover the 27 % was not localized in a manner that would cause one to contemplate a particular, conserved sequence associated with some function, but was distributed throughout.

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[26] Au Young '391 patent, column 4, lines 16-17

[27] Au Young '391 patent, column 4, lines 62-65

It is important to bear in mind that this alignment was on a deduced sequence. One can deduce a pseudogene however that still does not indicate that there is a protein in nature. For example, the comparison of the chicken sequence to SCAH-2 in the last two rows of Au Young '136, Figure 3 does not indicate to one of ordinary skill that SCAH-2 has stem cell antigen function.

At most, Au Young may have provided an invitation for further research to ultimately determine whether a putative protein exists and functions as a stem cell antigen. Fundamental gene and protein discovery would take place before any antibodies would be raised.

Second, Au Young speculated that the SCAH-2 protein might function like a Ly-6 molecule.[28] Scientifically, it was not established that SCAH-2 is in fact associated with Ly-6, neither was there a reasonable expectation that it is.

Moreover, even if SCAH-2 were a member of the Ly 6 family, there is no common function associated with the disparate members of the Ly-6 family. For example, some Ly-6 molecules are cell surface molecules that are involved in signal transduction,[29] or cell adhesion.[30] Others are secreted molecules that are involved with neurotoxicity or cytotoxicity,[31] or diseases unrelated to cancer.[32]

Given the broad range of potential Ly-6 functions, it would not have been credible to one of ordinary skill to extrapolate a particular meaningful function of SCAH-2 based on the other members of the Ly-6 family. Once again, at most, Au Young may provide an invitation for further research to ultimately determine whether it functions like Ly-6, and if so which of the numerous disparate functions. Even if there were an invitation for experimentation, such experimentation would not have included the raising of antibodies

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[28] Au Young '391 patent at column 2, lines 16-19; column 13, lines 41-47; column 16, lines 14-17; column 28, lines 13-21

[29] e.g., Gumley, et al., 1995, Immunol and Cell Biol, 73(4):277-96

[30] e.g., Brakenhoff, et al., 1995, J Cell Biol, 129(6):1677-1689

[31] e.g., Tsetlin, 1999, Eur J Biochem, 264:281-286

[32] e.g., Fischer et al., 2001, Human Mol Genet, 10(8):875-880

before a protein is credibly determined to actually occur in nature. Fundamental gene and protein discovery would take place before any antibodies would be raised.

6. Assumption: **That every possible antibody was, in fact, raised, or that one might have raised an antibody that might have had the properties of the present claims**

Fact: **Au Young raised no antibodies whatsoever.**

There is absolutely no evidence that antibodies such as those claimed in the present case, e.g., a monoclonal antibody which specifically binds to PSCA, existed in the prior art. Au Young does not disclose that she made any antibodies or deposited any hybridomas. Furthermore, the presently claimed antibodies are not obvious because it is not obvious to raise antibodies to a protein that is not known to exist in nature. Nothing disclosed to one of ordinary skill in March 1997, Au Young or otherwise in the art, that there truly was a SCAH-2 gene, protein, or that there was something scientifically meaningful to do with an antibody to such protein. As noted above in the discussion of Assumption 5, in this fact situation, raising of antibodies is not a method by which one would confirm existence of the putative protein.

At best, Au Young might have been an invitation to further experimentation in order to resolve the discovery issues regarding SCAH-2. If one were motivated to conduct research on SCAH-2 due to Au Young, initial acts would attempt to confirm existence of the nucleic acid sequence, such as by gene cloning. Moreover, further experimentation is required in order to determine any scientific meaning to the antibodies about which Au Young prophesied. As it is Au Young's comments about antibodies have no scientific meaning whatsoever. Without using hindsight based on PSCA and in view of the ambiguities of in Au Young, I cannot say that Au Young would even rise to an invitation for further experiments.

There is a "boilerplate" discussion of antibodies in Au Young (e.g., columns 13-15). Other than sequences, Au Young presents two Figures regarding SCAH-2 data: Figure 5 which "shows the hydrophobicity plot for SCAH-2 (SEQ ID NO: 2) generated

using MAC DNASIS software",[33] and Figure 7 which "shows an isoelectric plot for SCAH-2 (SEQ ID NO: 2) generated using MACDNASIS software."[34]. However, a very limited antibody discussion references Figure 5[35] and no reference is made to Figure 7. The sole mention of Figure 7 is in the Brief Description of the Figures.[36] Au Young draws no conclusion whatsoever from this data.

One cannot tell which SCAH-2 protein or proteins Au Young used to obtain this information. Furthermore, as this data is predicated on a deduced protein from a nucleic acid assembly, the protein, whatever its sequence, may not exist at all. This disclosure does nothing to resolve whether a protein truly exists.

In March 1997 one would *not* have been motivated to take Au Young's disclosure, and then modify it to yield the presently claimed antibodies. One would not

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[33] Au Young '391 patent, column 3

[34] Au Young '391 patent, column 3

[35] The passage reads:

> X Production of SCAH Specific Antibodies
>
> SCAH proteins purified using PAGE electrophoresis (Maniatis, supra) are used to immunize rabbits using standard protocols and to produce antibodies. The amino acid sequence translated from scah-1 or scah-2 is analyzed using DNASTAR software 9DNAStar Inc) to determine regions of high immunogenicity and a corresponding oligopolypeptide is synthesized and used to raise antibodies by means known to those of skill in the art. Analysis to select appropriate epitopes, such as those near the C-terminus or in hydrophilic regions is described by Ausubel FM et al (supra) and shown in FIGS. 4 and 5.
>
> Typically, the oligopeptides are 15 residues in length, synthesized using an Applied Biosystems Peptide Synthesizer Model 431A using fmoc-chemistry, and coupled to keyhole limpet hemocyanin (KLH, Sigma) by reaction with M-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS; Ausubel FM et al., supra). Rabbits are immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. The resulting antisera are tested for antipeptide activity, for example, by binding the peptide to plastic, blocking with 1% BSA, reacting with rabbit antisera, washing, and reacting with radioiodinated, goat anti-rabbit IgG.

Au Young '391, column 28, lines 27-49. *Note*, Figure 4 of Au Young is on SCAH-1.

[36] Au Young '391 patent, col. 3

in March 1997, or now, begin to synthesize random fragments of a putative protein before conducting fundamental gene discovery.[37]

Accordingly, Au Young did not disclose every element of the claimed invention, nor even elements such an expressed protein that would be needed to disclose the elements of the invention, and thus does not anticipate the claimed antibodies. Thus, the prior art in March 1997 did not allow one to make antibodies to SCAH-2.

Even if Au Young taught generally how to make an antibody, clearly Au Young does not teach making all antibodies to SCAH-2. Here one would need to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result. The prior art gave no indication of which parameters are critical and no direction as to which of many possible choices is likely to be successful. I understand that this fact pattern is one that does not result in obviousness.[38]

Much further experimentation was required in order to move from the disclosure of Au Young to the point of known and scientifically describable subject matter. There is essentially a total lack of direction or guidance presented about, e.g., the existence of any SCAH-2 gene, protein, function, expression or antibodies directed thereto. There is not even one actual example. In no way whatsoever did Au Young confirm the existence of any SCAH-2 gene or protein in nature. Given the lack of any confirmatory data, the predictability of the subject matter discussed by Au Young is almost zero.

Furthermore, the presently claimed antibodies are not obvious as there is no reason one of ordinary skill at that time would assess the Au Young disclosure as creating a meaningful expectation of success that there truly was a SCAH-2 gene, reading frame, protein, or that there was something scientifically meaningful to do with an antibody to such protein.

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[37] Au Young only prophetically, generically described making antibodies which bind any SCAH-1 or SCAH-2 polypeptide. For example, Au Young generally states producing an antibody using "an amino acid sequence consisting of at least five amino acids, preferably at least 10 amino acids" (column 13, lines 67, and column 14, line 1). However, this offered no guidance to those skilled in the art as Au Young failed to specify which particular 5 or 10 amino acid sequence may be used to produce the antibodies.

[38] In re O'Farrell, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988)

In sum, Au Young fails to disclose each of the elements of the claimed invention. Specifically, speaking as one of ordinary skill in the art as of March 1997, Au Young failed to disclose or suggest the actual existence of the following elements:

- Any SCAH-2 gene
- Any SCAH-2 protein
- The exact sequence of Applicant's PSCA protein
- A reading frame in the SCAH-2 nucleic acid sequence, let alone the correct reading frame for the PSCA protein of the present claims
- That a protein was truly encoded by any said reading frame, i.e., nothing eliminated the possibility that any gene of Au Young is a pseudogene.
- Failing to disclose any protein, it failed to disclose anything about such protein that was so meaningful that an antibody would be raised to it
- That every single possible antibody was, in fact, raised, or that one might have raised an antibody that might have had the properties of the present claims.

Nothing in the Au Young disclosure manifests to one of skill in the art that Au Young had a SCAH-2 gene, protein or antibody having the features set forth in that application. Nothing was isolated and/ or purified, and nothing was deposited with a public depository. Speaking as one of ordinary skill at that time, nothing about SCAH-2 appears from the Au Young disclosure to have actually been in possession of the applicant Au Young as of March 1997. The subject matter of the present claims was neither disclosed nor made able to be used by the Au Young disclosure.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18

of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at Santa Monica, California on July 16, 2003.

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PROFILE

Pharmaceutical research leader with extensive experience in novel target identification and validation, screen development and small molecule drug discovery, with expertise in oncology, immunology and inflammation. Skilled in motivating, developing, hiring, managing and building scientific teams to expedite novel drug candidate discovery for clinical trial consideration. Generate high level of performance through leadership, example and organization. Self-motivated strategic planner, with long range creative vision for addressing unmet clinical need with new therapeutics for immunological/inflammatory diseases and cancer.

EDUCATION

Ph.D.	University of Miami (Immunology and Microbiology)	**1986**
B.A.	University of California, Berkeley (Genetics)	**1980**

HONORS, AWARDS, SCHOLARSHIPS AND FELLOWSHIPS

Bristol-Myers Squibb Excellence Awards	**1996 - 2002**
NIH Postdoctoral Fellowship (F32-CA08316), University of Virginia	**1987 - 1990**
Presidential Scholarship, University of Miami	**1981 - 1986**
Honor Society, University of California, Berkeley	**1978 - 1980**

PROFESSIONAL EXPERIENCE

AGENSYS, INC. **2003 -**
Santa Monica, CA

Director, Cancer Research

Direct a research group including 20 scientists (Ph.D. and associates) to identify, validate and develop novel targets for the generation of new therapeutics for cancer. Prioritize in-house portfolio for evaluation of targets for either monoclonal antibody development or for alliances for small molecule development or vaccine generation. Report to the Chief Scientific Officer.

- Establish teams for the validation of targets using RNAi knockdown technologies and over-expression systems to evaluate novel genes for establishing new monoclonal antibody based cancer therapies
- Identify outside collaborators for possible alliances on propritetary targets to develop small molecule and vaccine approaches

BRISTOL-MYERS SQUIBB PHARMACEUTICAL RESEARCH INSTITUTE **1990 - 2003**
Princeton, NJ (in Seattle, WA from 1990-1997)

Associate Director, Immunology and Oncology Drug Discovery (1999 - 2003)

Directed a research group including 25 scientists (Ph.D. level and associates) to identify, validate and develop novel targets for therapeutic intervention in both immunological/inflammatory diseases and cancer. Managed annual research budget for group ($250K) for laboratory operations, travel and training of scientific staff. Senior leader guiding the direction of the research effort in all pre-clinical drug discovery phases, including administrative functions, reporting to the Vice President of Immunology and Oncology Drug Discovery.

- Established a research group to identify novel targets for therapeutic intervention in both immunological/inflammatory diseases and cancer. Group developed reagents, assays, screens and analyses on over fifteen targets for future drug discovery projects
- Validated novel targets through bioinformatics, microarray technologies, Taqman for expression profiling, transgenic mouse development and analysis, flow cytometry, full-length cloning, monoclonal antibody generation and general protein expression/purification
- Generated eight new screening assays (enzymes, protein-protein interactions, receptor systems) in 1.5 years with reduced cycle time (3-6 month turnaround time) from target validation to screening campaign
- Transitioned an early-phase project on Itk kinase to full-phase status in 1999 (screening campaign, lead identification, followed by significant chemistry support for SAR), taking a small molecule inhibitor to preclinical animal model testing stages and identifying efficacious compounds
- In-licensed a project on p38 from an external partner at an early phase, then transitioned it to full-phase status (1999). Developed a small molecule drug candidate (2001) for IND toxicology and phase I study
- Developed a Src kinase project (1997-2000) in immunology before transitioning program to Oncology, with discovery of an optimized small molecule currently ready for phase I studies
- Co-chaired the Exelixis Oncology alliance, established to identify new targets for cancer. Nine new targets for oncology were identified in 1.5 years, and three high throughput assays were established
- Served on immunology/inflammation licensing team for identifying outside opportunities, and served on pulmonary licensing team and subcommittees for early-stage external technologies. Efforts led to the in-licensing of the p38 project and licenses for using inflammatory target technologies

Principal Scientist, Immunological Diseases (1997 - 1999)

Established a Signal Transduction group to identify small molecule therapeutics to treat immunological and inflammatory disorders. Group included 4 Ph.D. level investigators and 11 associate scientists involved in projects relating to targeting intracellular signaling components for identification of new drug candidates

- Established and developed high throughput screens for 5 kinases, 1 phosphatase and 2 protein-protein interactions, and directed full and early-phase projects and various exploratory projects
- Screened Itk kinase, identified selective leads, developed compounds with chemistry support to isolate optimized pre-clinical candidates with efficacy in animal models of inflammation. Prepared patent application for novel drug series

- Identified lead compounds for Lck kinase, analyzed and characterized potent analogs in disease models for immunosuppression and inflammation

Senior Research Investigator II, Immunodeficiency and Immunomodulation (1993 - 1997)
Seattle, WA (former Oncogen biotechnology company purchased by Bristol-Myers Squibb Company)

- Generated antibody fragments from CD2-specific antibodies for use as biologic therapeutics for immunological/inflammatory indications
- Discovered a novel focal adhesion kinase (FAK)-related tyrosine kinase substrate (fakB), as well as analyzed other signal transduction molecules for potential drug targeting

Senior Research Investigator I, Immunodeficiency and Immunomodulation (1990 - 1993)
Seattle, WA (former Oncogen biotechnology company purchased by Bristol-Myers Squibb Company)

UNIVERSITY OF VIRGINIA, DEPARTMENT OF MICROBIOLOGY AND CANCER CENTER **1986 - 1990**
Charlottesville, VA

Postdoctoral fellow, Oncology (advisor: J. Thomas Parsons, Ph.D.)

- Commercialized six monoclonal antibodies to FAK, tensin, p120^{ctn}, phosphotyrosine and cortactin

PROFESSIONAL AFFILIATIONS

American Association of Immunologists
American Society for Microbiology
American Association for the Advancement of Science

AD HOC EDITORIAL ACTIVITY

Journal of Immunology
JI: Cutting Edge
Journal of Clinical Investigation
Journal of Biological Chemistry
Proc. Natl. Acad. Sci. USA
Molecular and Cellular Biology
Oncogene
Journal of Cellular Physiology
Antiviral Chemistry & Chemotherapy
Blood

PATENTS AND INVENTIONS

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Chang, H., W-P. Yang, Y. Wu, G. S. Whitney, J. J. Perez-Villar and S. B. Kanner. Cloning and expression of human SLAP-2: a novel SH2/SH3 domain-containing human SLAP homologue having immune cell-specific expression. WO-0242457; June, 2002

Kanner, S. B., A. B. Reynolds, S. J. Parsons and J. T. Parsons. Monoclonal antibodies to $p125^{FAK}$, $p120^{ctn}$, cortactin, $pp60^{src}$ and tensin. Licensed and commercialized from the University of Virginia to Upstate/Cell Signaling Solutions

Kanner, S. B., A. B. Reynolds and J. T. Parsons. Monoclonal antibody 6G9 to phosphotyrosine. Licensed and commercialized from the University of Virginia to Covance, Inc./Berkeley Antibody Company

INVITED PRESENTATIONS

Regulated association between the SH3 domain of the Emt/Itk tyrosine kinase and multiple intracellular ligands. Lymphocyte Signal Transduction Workshop, Santorini, Greece (October, 2000)

Signal transduction through the T-lymphocyte receptors CD2 and LFA-1. Sugen, South San Francisco, California (June, 1996)

Lymphocyte antigen receptor activation of a novel FAK-related tyrosine kinase substrate. Lymphocyte Activation Meeting, Keystone Symposia on Molecular and Cellular Biology, Keystone, Colorado (April, 1994)

T-cell signaling via integrin receptors and immunoglobulin-superfamily molecules. University of Chicago, Committee on Immunology Seminar Series, Chicago, Illinois (March, 1994)

T-cell signaling through integrins and Ig superfamily receptors. Seattle Biomedical Research Institute, Seminar Series, Seattle, Washington (March, 1993)

β_2-integrin signaling in T-cells through PLCγ1 is TCR-dependent. Keystone Symposium on Phosphorylation/Dephosphorylation in Signal Transduction, Keystone, Colorado (January, 1993)

Regulation of TCR-induced PLCγ1 tyrosine phosphorylation by CD45. Plenary seminar at Biochemical Immunology Group Colloquium on the Structure and Function of the Leukocyte Common Antigen CD45, Edinburgh, Scotland (September, 1991)

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